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Nonalcoholic fatty liver disease is associated with insulin resistance in a young Hispanic population

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ABSTRACT

Objective. To investigate whether nonalcoholic fatty liver disease (NAFLD) is associated with insulin resistance (IR) in a young Hispanic population.

Methods. A cross-sectional study was performed in Bogotá, Colombia, during 2006 in 263 males from the Colombian Air Force (age range 29–54 years). Anthropometric measurements and biochemical determinations (glycemia, lipid profile, insulin, and HOMA-IR) were obtained in order to determine the presence of metabolic syndrome (MS) criteria and insulin resistance in this population. In addition, ultrasound studies were performed to evaluate the presence of NAFLD.

Results. NAFLD was detected in 26.6% ($n=70$) of the subjects. Thirty four individuals had complete MS criteria (48.5%). The presence of NAFLD was associated with higher insulin levels (11.0 ± 5.1 vs. 6.6 ± 3.6, $p=0.001$), and its prevalence increased from 11% ($n=8$), to 24% ($n=17$) to 64% ($n=45$) from the lowest to the highest HOMA-IR tertile. Body mass index, triglycerides and subcutaneous and visceral fat were found to be independent predictors of NAFLD.

Conclusions. These results suggest that NAFLD is associated with insulin resistance and extrahepatic adiposity in nondiabetic young Hispanic population.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is characterized by the accumulation of hepatic fat in patients without history of excessive alcohol consumption (Browning et al., 2004). This condition may progress to nonalcoholic steatohepatitis (NASH), liver cirrhosis and hepatocellular carcinoma (Angulo, 2005). A close association between NAFLD and insulin resistance (IR) has been reported (Marchesini et al., 2001a; Targher et al., 2007; Utzschneider and Kahn, 2006). Moreover, the prevalence of metabolic syndrome (MS) in NAFLD is very high, and it has been suggested that IR could be not only a mere occasional finding, but also a pathogenic factor responsible for both MS and hepatic steatosis (Bugianesi et al., 2004).

A higher prevalence of hepatic steatosis has been described in Hispanic populations compared to Caucasic populations, and it has been proposed that this difference is caused by a higher prevalence of obesity and IR in these ethnic groups (Browning et al., 2004). Previously, our group reported that Colombian population had also a greater propensity to develop IR and MS at relatively lower levels of abdominal obesity (Garcia et al., 2006, 2007), which could be related to epigenetic adaptations forced by the abrupt urbanization process, the sedentary lifestyle and the consumption of high fat and calorie foods (Lopez-Jaramillo et al., 2008). It has been hypothesized that in this population, fetal programming in response to maternal malnutrition results in the development of fetus with an increased tendency to develop IR, with deficient hepatic, renal, cardiac and pancreatic anatomical structures, which might explain the increased risk for certain chronic diseases, including type 2 diabetes mellitus, renal and cardiac failure and cirrhosis observed in developing countries (Lopez-Jaramillo, 2009). In light of these observations, the aim of the present

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study was to determine whether NAFLD was associated with MS and IR markers in a young Hispanic population.

Methods

Study population

A cross-sectional study was performed in 263 officers (age range 29–54 years) from the Colombian Air Force personnel, who attended an annual medical examination in 2006. The study was approved by the Ethics Committee of the Nueva Granada Military University. Subjects who presented acute or chronic inflammatory diseases and/or cancer were excluded.

Procedures

A verbal interview aimed to determine cardiovascular risk factors and medication use was performed in all participants. All anthropometric measures were taken with participants wearing light clothes and no shoes. Weight was measured on a balance-beam scale and recorded to the nearest one hundredth of a gram. Height was measured to the nearest 0.5 cm. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Waist Circumference (WC) was measured in the standing position by applying a linen measuring tape horizontally midway between the iliac crest and the lower portion of the rib cage. The mean of those two measurements (recorded to the nearest 0.1 cm) was used to estimate visceral fat (Lohman et al., 1988). Blood pressure was measured following the recommendations of the European Society of Hypertension (O'Brien et al., 2003).

Ultrasonographic measures were performed by a radiologist using a Toshiba Nemio 4D digital ultrasound, with a 3.5 MHz convex transducer (Toshiba Medical Systems, Tustin, CA). The transducer was gently placed 1 cm above the umbilicus. Ultrasound-determined subcutaneous fat was defined as the distance between the skin and the external face of the rectus abdominal muscle, and visceral fat as the distance between the internal face of the same muscle and the anterior wall of the aorta (Ribeiro-Filho et al., 2003). NAFLD diagnosis was made in subjects with absent-to-low alcohol consumption (<30 g/day) using the following criteria: a) increase in liver echogenicity with respect to the kidney, b) low or absent visualization of the portal vessels, and c) presence of hepatomegaly (Csendes et al., 2004). A fasting blood sample was taken to determine glycemia, lipid profile, insulin, C-reactive protein and uric acid. A 75-g oral glucose test was performed. Glucose, triglycerides, total cholesterol, high density lipoprotein cholesterol, uric acid, γ-glutamyl transferase (GGT), ultra sensitive C-reactive protein and insulin were measured on a Hitachi 917 auto analyzer (Roche Diagnostics, Indianapolis, IN). MS diagnosis was defined according to the International Diabetes Federation (IDF) recommendations for Latin American populations (waist circumference >90 cm, together with two of the following criteria: fasting glucose>100 mg/dl (5.55 mmol/l), TG >150 mg/dl (1.70 mmol/l), high density lipoprotein cholesterol <50 mg/dl (1.30 mmol/l), blood pressure >130/85 mmHg) (Alberti et al., 2005). Insulin resistance was measured by homeostasis model assessment of insulin resistance (HOMA-IR) = [fasting insulin (μUI/ml) × fasting glucose (mmol/l) / 22.5]. The values were divided into tertiles and the prevalence of NAFLD for each of these tertiles was determined.

Statistical analyses

The results were analyzed using the SPSS 15.0 statistical program (SPSS Inc., Chicago, IL, 2007). Values were expressed as means ± SD. Comparisons between groups were performed with *t*-test. All variables were included in a logistic regression analysis to identify independent factors for NAFLD. Differences were considered statistically significant if $p<0.05$. ROC analyses were used to determine the best cutoff points of HOMA-IR index, and the waist perimeter that each identifies the presence of NAFLD. Spearman correlation test was used to evaluate the association between abdominal perimeter and insulin resistance.

Results

The anthropometric and biochemical characteristics of the 263 male individuals included are described in Table 1. None of the subjects had a history of alcohol consumption exceeding 14 drinks per week. NAFLD was detected by ultrasound examination in 70 subjects (26.6%). Only 34 of these individuals had complete MS criteria. Patients with NAFLD had a higher body mass index, waist perimeter, diastolic blood pressure, triglycerides, fasting plasma insulin, post-glucose load levels, uric acid, subcutaneous and visceral fats, and GGT values in comparison with subjects without NAFLD (Table 2). The prevalence of NAFLD increased from 11% ($n=8$), to 24% ($n=17$) to 64% ($n=45$) from the lowest to the highest HOMA-IR tertile (Fig. 1).

The logistic regression model applied to the entire sample, established as predictors of NAFLD the body mass index, triglycerides, high density lipoprotein cholesterol, subcutaneous fat and visceral fat (Table 3). Using ROC curves analyses, a HOMA-IR index of 1.74 (sensitivity 74.3% and specificity 73.1%) (Fig. 2A) and a WC of 92 cm (sensitivity 75% and specificity 74%) (Fig. 2B), were identified as the best cut-off points related to the presence of NAFLD.

Table 1
Baseline and biochemical characteristic of 263 liver disease-free subjects included in the study at the Aerospace Medical Center from the Colombian Air Force, Bogotá, Colombia, 2006.

	Subjects ($n=263$)
Age (years)	38.6 (5.8)
Body mass index (kg/m^2)	24.7 (2.85)
Waist (cm)	88.9 (7.35)
Subcutaneous fat (mm)	16.4 (5.6)
Visceral fat (mm)	31.1 (13.6)
Systolic blood pressure (mmHg)	114.8 (14.6)
Diastolic blood pressure (mmHg)	72.6 (10.6)
Triglycerides (mmol/l)	1.98 (1.18)
High density lipoprotein-cholesterol (mmol/l)	1.17 (0.29)
Fasting glycemia (mmol/l)	5.07 (0.46)
Post-glucose load glucose (mmol/l)	4.65 (1.27)
C-reactive protein (mg/l)	2.8 (4.8)
γ-glutamyltransferase (U/l)	44.7 (52.04)
Insulin (pmol/l)	54.2 (31.2)
HOMA-IR index	1.8 (1.1)
Uric acid (μmol/l)	389.0 (76.7)

Data expressed as mean (SD).

Discussion

In the present study individuals with NAFLD had higher prevalence of MS criteria (48.6% vs. 14%) compared to normal subjects. In addition, high density lipoprotein cholesterol levels, subcutaneous fat and visceral fat were identified as significant predictors of NAFLD

Table 2
Main characteristics of the 263 liver disease-free subjects included in the study at the Aerospace Medical Center from the Colombian Air Force, Bogotá, Colombia, 2006, according to the presence of nonalcoholic fatty liver disease (NAFLD).

	Subjects with NAFLD ($n=70$)	Subjects without NAFLD ($n=193$)	*P* value
Age (years)	39.3 (5.3)	38.3 (5.9)	0.13
Body mass index (kg/m^2)	26.8 (2.5)	23.9 (2.5)	<0.01
Waist (cm)	94.4 (5.8)	86.8 (6.7)	<0.01
Subcutaneous fat (mm)	19.4 (6.7)	15.2 (4.7)	<0.01
Visceral fat (mm)	40.8 (12.7)	27.4. (12.2)	<0.01
Systolic blood pressure (mmHg)	116.1 (14.4)	113.2 (13.9)	0.13
Diastolic blood pressure (mmHg)	74.0 (9.4)	71.2 (9.9)	0.04
Triglycerides (mmol/l)	2.69 (1.54)	1.72 (0.89)	<0.01
HDL (mmol/l)	1.00 (0.19)	1.23 (0.30)	<0.01
Fasting glycemia (mmol/l)	5.13 (0.44)	5.05 (0.46)	0.19
Post-glucose load glucose (mmol/l)	5.06 (1.53)	4.50 (1.13)	<0.01
C-reactive protein (mg/l)	3.7 (6.3)	2.5 (4.2)	0.08
γ-glutamyltransferase (U/l)	67.1 (81.5)	36.6 (32.5)	<0.01
Insulin (pmol/l)	76.4 (35.4)	45.8 (25.0)	<0.01
HOMA-IR index	1.41 (3.1)	0.51 (1.89)	<0.01
Uric acid (μmol/l)	416.4 (71.2)	374.7 (71.3)	<0.01

Data expressed as mean (SD). HDL, High density lipoprotein.